

WHAT IS CLAIMED IS:

1. A peptide nucleic acid conjugate comprising:
a peptide nucleic acid;
said peptide nucleic acid having a backbone;
said backbone having an amino end, a carboxyl end, and
a plurality of amino groups;
said amino groups each having a tethered nucleobase;
and a conjugate bound to said peptide nucleic acid either
directly or through a linking moiety.

2. A peptide nucleic acid conjugate of claim 1
wherein said conjugate is bound through said linking moiety
to at least one of said backbone, said tether, or said
nucleobase.

3. A peptide nucleic acid conjugate of claim 1
wherein said conjugate is bound to said backbone.

4. A peptide nucleic acid conjugate of claim 3
wherein said conjugate is bound to at least one of said
amino end or said carboxyl end of said backbone.

5. A peptide nucleic acid conjugate of claim 1
wherein said conjugate is bound to said nucleobase or said
tether.

Nielsen et al.

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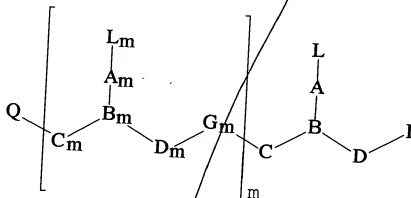
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6. A peptide nucleic acid conjugate of claim 1 wherein said conjugate is a reporter enzyme, a reporter molecule, a steroid, a carbohydrate, a terpene, a peptide, a protein, an aromatic lipophilic molecule, a non aromatic lipophilic molecule, a phospholipid, an intercalator, a cell receptor binding molecule, a crosslinking agent, a water soluble vitamin, a lipid soluble vitamin, an RNA cleaving complex, a metal chelator, a porphyrin, an alkylator, or a polymeric compound selected from polymeric amines, polymeric glycols and polyethers.

7. A peptide nucleic acid conjugate of the formula:



wherein:

m is an ineteger from 1 to about 50;

L and L_m independently are R¹²(R¹³)_n; wherein:

R¹² is hydrogen, hydroxy, (C₁-C₄)alkanoyl, a

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naturally occurring nucleobase, a non-naturally occurring nucleobase, an aromatic moiety, a DNA intercalator, a nucleobase-binding group, a heterocyclic moiety, a reporter ligand, or a conjugate;

5

provided that at least one of R^{12} is a naturally occurring nucleobase, a non-naturally occurring nucleobase, a DNA intercalator, or a nucleobase-binding group;

R^{13} is a conjugate; and

a is 0 or 1;

C and C_m independently are $(CR^6R^7)_y$; wherein:

R^6 and R^7 independently are hydrogen, a side chain of a naturally occurring alpha amino acid, (C_2-C_6) alkyl, aryl, aralkyl, heteroaryl, hydroxy, (C_1-C_6) alkoxy, (C_1-C_6) alkylthio, a conjugate, NR^3R^4 , SR^5 or R^6 and R^7 taken together complete an alicyclic or heterocyclic system;

15

wherein R^5 is hydrogen, a conjugate, (C_1-C_6) alkyl, hydroxy-, alkoxy-, or alkylthio-substituted (C_1-C_6) alkyl; and

20

R^3 and R^4 independently are hydrogen, a conjugate, (C_1-C_4) alkyl, hydroxy- or alkoxy- or alkylthio-substituted (C_1-C_4) alkyl, hydroxy, alkoxy, alkylthio or amino;

25

D and D_m independently are $(CR^6R^7)_z$;

Sub 13
cont

each of y and z is zero or an integer from 1 to 10, wherein the sum $y + z$ is greater than 2 but not more than 10;

G_m is independently $-NR^3CO-$, $-NR^3CS-$, $-NR^3SO-$, or $-NR^3SO_2-$ in either orientation;

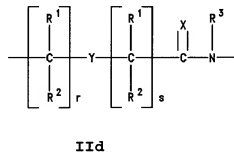
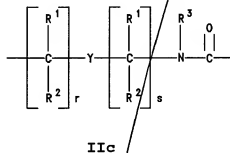
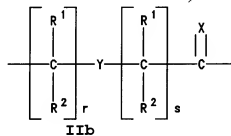
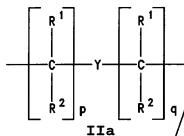
each pair of $A-A_m$ and $B-B_m$ are selected such that:

(a) A or A_m is a group of formula (IIa), (IIb) or

(IIc) and B or B_m is N or R^3N^+ ; or

(b) A or A_m is a group of formula (IIId) and B or B_m is

CH;



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wherein:

X is O, S, Se, NR^3 , CH_2 or $\text{C}(\text{CH}_3)_2$;

Y is a single bond, O, S or NR^4 ;

each of p and q is zero or an integer from 1 to 5, the
5 sum p+q being not more than 10;

each of r and s is zero or an integer from 1 to 5, the
sum r+s being not more than 10;

Sub 3 cont.
10 R^1 and R^2 independently are hydrogen, $(\text{C}_1\text{-C}_4)\text{alkyl}$,
hydroxy-substituted $(\text{C}_1\text{-C}_4)\text{alkyl}$, alkoxy-substituted $(\text{C}_1\text{-C}_4)\text{alkyl}$,
alkylthio-substituted $(\text{C}_1\text{-C}_4)\text{alkyl}$, hydroxy,
alkoxy, alkylthio, amino, halogen or a conjugate;

I is $-\text{NR}^8\text{R}^9$ or $-\text{NR}^{10}\text{C}(\text{O})\text{R}^{11}$; wherein:

15 R^8 , R^9 , R^{10} and R^{11} independently are hydrogen,
alkyl, an amino protecting group, a reporter
ligand, an intercalator, a chelator, a peptide, a
protein, a carbohydrate, a lipid, a steroid, a
nucleoside, a nucleotide, a nucleotide
diphosphate, a nucleotide triphosphate, an
oligonucleotide, an oligonucleoside, a soluble
20 polymer, a non-soluble polymer or a conjugate;

Q is $-\text{CO}_2\text{H}$, $-\text{CO}_2\text{R}^8$, $-\text{CO}_2\text{R}^9$, $-\text{CONR}^8\text{R}^9$, $-\text{SO}_3\text{H}$, $-\text{SO}_2\text{NR}^{10}\text{R}^{11}$ or
an activated derivative of $-\text{CO}_2\text{H}$ or $-\text{SO}_3\text{H}$; and

wherein at least one of R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , R^8 ,
 R^9 , R^{10} , R^{11} , R^{12} and R^{13} is a conjugate wherein said conjugate
25 is a reporter enzyme, a reporter molecule, a steroid, a

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carbohydrate, a terpene, a peptide, a protein, an aromatic lipophilic molecule, a non aromatic lipophilic molecule, a phospholipid, an intercalator, a cell receptor binding molecule, a crosslinking agent, a water soluble vitamin, a lipid soluble vitamin, an RNA cleaving complex, a metal chelator, a porphyrin an alkylator, or a polymeric compound selected from polymeric amines, a polymeric glycols and polyethers; and

wherein said conjugate optionally includes a linking moiety.

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SUB 13
8. A peptide nucleic acid conjugate of claim 37 wherein said conjugate includes a linking moiety.

B
9. A peptide nucleic acid conjugate of claim 37 wherein at least one group R^{12} is a conjugate.

SUB 14
10. A peptide nucleic acid conjugate of claim 7 wherein at least one group R^{13} is a conjugate.

B
11. A peptide nucleic acid conjugate of claim 37 wherein at least one of R^1 , R^2 or R^3 is a conjugate.

F
SUB 15
12. A peptide nucleic acid conjugate of claim 39 wherein at least one of said $A-A_m$ groups include at least one of R^1 , R^2 , and R^3 .

13. A peptide nucleic acid conjugate of claim 11³⁹ wherein at least one of said B-B_m groups or said G-G_m groups include at least one group R³.

14. A peptide nucleic acid conjugate of claim 12³⁷ wherein at least one of R⁸, R⁹, R¹⁰ and R¹¹ is a conjugate.

15. A peptide nucleic acid conjugate of claim 14³⁷ wherein at least one of said groups Q or I include at least one of groups R⁸, R⁹, R¹⁰ and R¹¹.

16. A peptide nucleic acid conjugate of claim 15³⁷ wherein at least one of R³, R⁴, R⁵, R⁶ and R⁷ is a conjugate.

17. A peptide nucleic acid conjugate of claim 16 wherein at least one of said groups D-D_m, or C-C_m include at least one of R³, R⁴, R⁵, R⁶ and R⁷.

18. A peptide nucleic acid conjugate of claim 17³⁷ wherein m is from 1 to about 200.

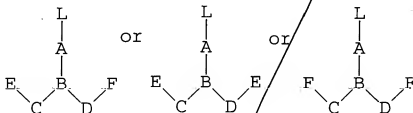
19. A peptide nucleic acid conjugate of claim 18³⁷ wherein m is from 1 to about 50.

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wherein m is from 1 to about 20.

21. A compound having one of the following formulas:



wherein:

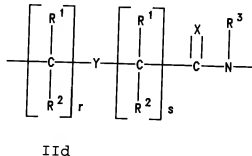
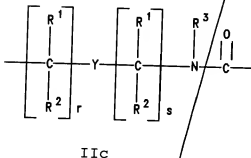
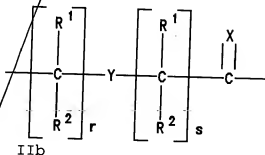
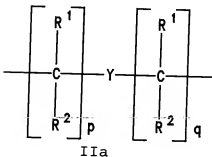
5 L is $R^{12}(R^{13})_a$; wherein:

R¹² is hydrogen, hydroxy, (C₁-C₄)alkanoyl, a naturally occurring nucleobase, a non-naturally occurring nucleobase, an aromatic moiety, a DNA intercalator, a nucleobase-binding group, a heterocyclic moiety, a reporter ligand, or a conjugate and at least one of R¹² is a naturally occurring nucleobase, a non-naturally occurring nucleobase, a DNA intercalator, or a nucleobase-binding group;

15 R^{13} is a conjugate; and
a is 0 or 1;

A and B are selected such that:

- (a) A is a group of formula (IIa), (IIb) or (IIc) and B is N or R^3N^+ ; or
 (b) A is a group of formula (IId) and B is CH;



5 where:

X is O, S, Se, NR^3 , CH_2 or $C(CH_3)_2$;

Y is a single bond, O, S or NR^4 ;

p and q independently are zero or an integer from 1 to 5, the sum p+q being not more than 10;

10 r and s independently are zero or an integer from 1 to 5, the sum r+s being not more than 10;

R^1 and R^2 independently are hydrogen, (C_1-C_4) alkyl,

hydroxy-substituted (C₁-C₄)alkyl, alkoxy-substituted (C₁-C₄)alkyl, alkylthio-substituted (C₁-C₄)alkyl, hydroxy, alkoxy, alkylthio, amino, halogen or a conjugate;

C is (CR⁶R⁷)_y;

5 D is (CR⁶R⁷)_z; wherein:

R⁶ and R⁷ independently are hydrogen, a side chain of a naturally occurring alpha amino acid, (C₂-C₆)alkyl, aryl, aralkyl, heteroaryl, hydroxy, (C₁-C₆)alkoxy, (C₁-C₆)alkylthio, a conjugate, NR³R⁴ and SR⁵ or R⁶ and R⁷ taken together complete an alicyclic or heterocyclic system;

R³ and R⁴ independently are hydrogen, a conjugate, (C₁-C₄)alkyl, hydroxy- or alkoxy- or alkylthio-substituted (C₁-C₄)alkyl, hydroxy, alkoxy, alkylthio or amino; and

R⁵ is hydrogen, a conjugate, (C₁-C₆)alkyl, hydroxy-, alkoxy-, or alkylthio- substituted (C₁-C₆)alkyl;

each of y and z is zero or an integer from 1 to 10, the sum y + z being greater than 2 but not more than 10;

10 E independently is COOH, CSOH, SOOH, SO₂OH or an activated or protected derivative thereof;

F independently is NHR³ or NPgR³, where Pg is an amino protecting group; and

25 at least one of R¹, R², R³, R⁴, R⁵, R⁶, R⁷, R¹², and R¹³ is a conjugate wherein said conjugate is a reporter enzyme, a reporter molecule, a steroid, a carbohydrate, a terpene, a peptide, a protein, an aromatic lipophilic molecule, a non aromatic lipophilic molecule, a phospholipid, an intercalator, a cell receptor binding molecule, a crosslinking agent, a water soluble vitamin, a lipid soluble vitamin, an RNA cleaving complex, a metal chelator, a porphyrin an alkylator, or a polymeric compound selected from polymeric amines, polymeric glycols and polyethers; and wherein said conjugate optionally includes a linking moiety.

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22. A peptide nucleic acid conjugate of claim 21
wherein said conjugate includes a linking moiety.

23. A peptide nucleic acid conjugate of claim 21
wherein R¹² is a conjugate.

24. A peptide nucleic acid conjugate of claim 21
wherein R¹³ is a conjugate.

25. A peptide nucleic acid conjugate of claim 21
wherein at least one group R³ is a conjugate.

26. A peptide nucleic acid conjugate of claim 21
wherein at least one of said groups A or said groups B
include a conjugate.

27. A peptide nucleic acid conjugate of claim 21
wherein at least one of group R¹ or group R² is a conjugate.

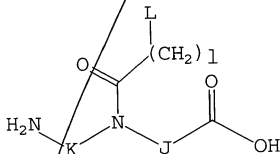
28. A peptide nucleic acid conjugate of claim 21
wherein at least one of R³, R⁴, R⁵, R⁶, and R⁷ is a conjugate.

29. A peptide nucleic acid conjugate of claim 21
wherein at least one of said groups C or said groups D
include a conjugate.

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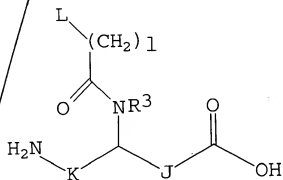
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30. A peptide nucleic acid conjugate comprising a plurality of PNA monomers wherein at least one of said PNA monomers has the formula:

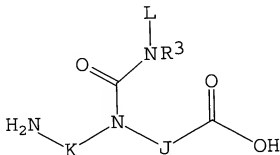


or formula:

5.



or formula:



wherein:

L is $R^{12}(R^{13})_a$; wherein:

R^{12} is hydrogen, hydroxy, (C_1-C_4) alkanoyl, a naturally occurring nucleobase, a non-naturally occurring nucleobase, an aromatic moiety, a DNA intercalator, a nucleobase-binding group, a heterocyclic moiety, a reporter ligand, or a conjugate and at least one of R^{12} is a naturally occurring nucleobase, a non-naturally occurring nucleobase, a DNA intercalator, or a nucleobase-binding group;

R^{13} is a conjugate; and

a is 0 or 1;

K is $(CR^6R^7)_z$;

J is $(CR^6R^7)_y$; wherein:

R^6 and R^7 are independently hydrogen, a side chain of a naturally occurring alpha amino acid, (C_2-C_6) alkyl, aryl, aralkyl, heteroaryl, hydroxy, (C_1-C_6) alkoxy, (C_1-C_6) alkylthio, a conjugate, NR^3R^4 and SR^5 or R^6 and R^7 taken together complete an alicyclic or heterocyclic system;

R^3 and R^4 independently are hydrogen, a conjugate, (C_1-C_4) alkyl, hydroxy- or alkoxy- or alkylthio-substituted (C_1-C_4) alkyl, hydroxy, alkoxy, alkylthio or amino;

R^5 is hydrogen, a conjugate, (C_1-C_6) alkyl, hydroxy-, alkoxy-, or alkylthio- substituted (C_1-C_6) alkyl;

each of y and z is zero or an integer from 1 to 10, the sum y + z being greater than 2 but not more than 10;

l is an integer from 1 to 5; and

at least one of R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , R^{12} , and R^{13} is a conjugate wherein said conjugate is a reporter enzyme, a reporter molecule, a steroid, a carbohydrate, a terpene, a peptide, a protein, an aromatic lipophilic molecule, a non aromatic lipophilic molecule, a phospholipid, an

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intercalator, a cell receptor binding molecule, a crosslinking agent, a water soluble vitamin, a lipid soluble vitamin, an RNA cleaving complex, a metal chelator, a porphyrin an alkylator, or a polymeric compound selected from polymeric amines, polymeric glycols and polyethers; and wherein said conjugate optionally includes a linking moiety.

31. A peptide nucleic acid conjugate of claim 30 wherein said conjugate includes a linking moiety.

32. A peptide nucleic acid conjugate of claim 30 wherein ~~R¹² is a conjugate~~.

33. A peptide nucleic acid conjugate of claim 30 wherein ~~R¹³ is a conjugate~~.

34. A peptide nucleic acid conjugate of claim 30 wherein at least one of R³, R⁴, R⁵, R⁶, and R⁷ is a conjugate.

35. A peptide nucleic acid conjugate of claim 30 wherein at least one of said group K or said group J includes a conjugate.

36. A peptide nucleic acid conjugate of claim 30 wherein said group R³ is a conjugate.

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